

REMARKS**I. Status of the Claims**

With this amendment, claims 9, 10, 24-40, 42-43, 49-60, 63-66, and 68-75 are pending in the present application and are under examination. Claims 1-8, 11-23, 41, 44-48, 61-62, and 67 have been canceled. Claims 9 and 10 have been amended.

II. Rejections Under 35 U.S.C. §103(a)

The Examiner has rejected claims 9, 10, 24-29, 33, 39, 40, 42, 43, 49-52, 54-60, 63-66, and 68-75 as allegedly being unpatentable over Shiver *et al.*, Haas *et al.*, Persson *et al.*, and Novitzky *et al.*.

The Examiner has rejected claims 9, 10, 24-29, 33, 39, 40, 42, 43, 49-60, 63-66, and 68-75 as allegedly being unpatentable over Shiver *et al.*, Haas *et al.*, Novitzky *et al.*, and Persson *et al.*, as applied to claims 9, 10, 24-29, 33, 39, 40, 42, 43, 49-52, 54-60, 63-66, and 68-75, in further view of March *et al.*.

The Examiner has rejected claims 9, 10, 24-40, 42, 43, 49-52, 54-60, 63-66, and 68-75 as allegedly being unpatentable over Shiver *et al.*, Haas *et al.*, Novitzky *et al.*, and Persson *et al.*, as applied to claims 9, 10, 24-29, 33, 39, 40, 42, 43, 49-52, 54-60, 63-66, and 68-75, in further view of Kapitonov *et al.* The Examiner alleges that based on the teachings of Shiver *et al.* and Schneider *et al.* it would have been obvious to one of skill in the art to eliminate any “ATTTA” sequences, wild-type or modified.

In the Advisory Action dated May 4, 2009, the Examiner asserted that the Applicant’s arguments in the reply to the Final Office Action from April 9, 2009, were directed to Figure 5 and not the claims, to which the rejections were directed.

Applicant respectfully traverses each of the rejections and their supporting remarks. A *prima facie* obviousness action has not been established. The Examiner has asserted that Shiver *et al.* teach the removal of INS sequences by pointing to the statement in Shiver *et al.* regarding removal of “ATTTA” sequences. The Examiner has further asserted that it would be obvious to apply two steps to optimize the expression by first optimizing codons and then removing “ATTTA” sequences as taught by Shiver *et al.* While removal of “ATTTA” sequences may

constitute removal of INS sequences, this does not correspond to the changes to the sequences made by the inventors that resulted in the claimed SEQ ID NOs: 3 and 4 as shown by Figures 5 and 6. SEQ ID NOs: 20 and 21 correspond to the codon optimized *gag* sequences generated by the inventors (i.e., after performing the first of two optimization steps). Figures 5 and 6 shows the changes made by the inventors in their second optimization step of removing instability sequences (i.e., the changes from SEQ ID NOs: 20 and 21 to generate the claimed SEQ ID NOs: 3 and 4. The resulting nucleic acid sequence differences between SEQ ID NOs: 20 and 3 or SEQ ID NOs: 21 and 4 are shown in Figures 5 and 6 in the application to illustrate the changes (boxed frames) in the nucleic acid coding sequence of the *gag* gene by removal of the instability elements *after* the AT-rich wild-type codons had been replaced with those of GC-rich highly expressed human genes. Thus, the second step performed by the inventors to generate the claimed invention did not involve directly elimination of any “ATTTA” sequences as taught by Shiver *et al.* Thus, the changes in the second optimization step that resulted in the claimed SEQ ID NOs: 3 and 4 do not appear to be the changes referred to in Shiver *et al.* (“ATTTA”) as most of the changes do not involve As or Ts. Therefore, the Examiner’s reference to Shiver *et al.* teaching of changing “ATTTA” does not appear to constitute a teaching or suggestion to make the changes to the sequences made as disclosed in SEQ ID NOs: 3 and 4 and further illustrated in Figures 5 and 6 since the step taught by Shiver *et al.* that the Examiner has asserted would be an obvious second step to perform after codon optimization does not correspond to the second step performed by the inventors.

Furthermore, even if it were obvious to optimize the *gag* coding sequences for improved expression, there are many ways to improve the expression of genes which will change the nucleic acid sequence, including, but not limited to, selecting codon usage from differently efficient expressed genes from a variety of species; optimizing the codon usage of the whole gene or only a fraction thereof; complete or incomplete removal of inhibitory sequences, internal signal sequences, and splicing signals; implementing various start and stop codon sequence environments; and the order of execution of these nucleic acid sequence modifications. In addition, there are many possible strains from which an HIV subtype C *gag* coding sequence may be obtained besides those that the inventors chose, which could also affect the final modified sequence.

Thus, the resulting claimed sequences as disclosed in SEQ ID NOs: 3 and 4 are not obvious, since although the amino acid sequence of the HIV Gag protein was previously disclosed, the potential number of nucleic acid sequences for increased expression of the HIV Gag protein is representing a broad genus given that one of skill in the art could have selected from a significant number of different HIV-1 subtype C *gag* coding sequences as of the priority date, and one of skill in the art could have chosen from a number of different optimization techniques, each of which could have generated a different optimized sequence. Thus, even if it were obvious to optimize an HIV *gag* coding sequence, that would not render SEQ ID NOs: 3 or 4 obvious, as SEQ ID NOs: 3 and 4 are species of the genus of possible optimized HIV-1 subtype C *gag* coding sequences. See, e.g., *In re Deuel*, 51 F.3d 1552, 1558-59, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995), where the Federal Circuit stated, “[a] prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein.” The present situation is analogous as there are many possible modified HIV *gag* encoding sequences with also possibly diverse expression profiles, while the instant claims are directed to two particular polynucleotide sequences – SEQ ID NOs: 3 and 4.

Since the Examiner has not shown that the obviousness rejections teach or suggest the nucleic acid sequence modifications resulting in SEQ ID NOs: 3 and 4, and even if modification of an HIV-1 subtype C *gag* encoding sequence were obvious, the pending claims are a species of such modified coding sequences and are therefore not obvious over the genus of modified coding sequences. Applicants therefore respectfully request withdrawal of the three rejections under 35 U.S.C. 103(a) of claims 9, 10, 24-40, 42-43, 49-60, 63-66, and 68-75 under 35 U.S.C § 103(a).

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 223002109700. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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